Table SI. 5-LO protein expression in $CD34^+$ cells from healthy volunteers (n=6) and patients with PV (n=8) was calculated using densitometry and normalized to β-actin expression.

	Group			
Variable	Normal (n=6)	PV (n=8)	Two-tailed Mann-Whitney test	P-value
Ratio 5-LO/β-actin, median (IQR)	0.68 (0.46, 0.75)	1.17 (0.97, 1.32)	48	<0.001

The results are presented as medians and IQRs. Differences between groups were analyzed using a two-tailed Mann-Whitney test. 5-LO, 5-lipoxygenase; IQR, interquartile range; PV, polycythemia vera.

Table SII. Relative mRNA expression levels of 5-LO in $CD34^+$ cells from normal controls (n=10) and patients with PV (n=12) after normalization to GAPDH.

Variable	Group		Two-tailed Mann-Whitney test	P-value
	Normal (n=10)	PV (n=12)		
5-LO mRNA expression, median (IQR)	1.06 (0.64, 1.25)	3.64 (2.04, 4.70)	115	<0.001

The results are presented as medians and IQRs. Differences between groups were analyzed using a two-tailed Mann-Whitney test. 5-LO, 5-lipoxygenase; IQR, interquartile range; PV, polycythemia vera.

Table SIII. Plasma LTB4 levels in normal controls (n=10) and patients with PV (n=14).

Variable	Group		Two-tailed Mann-Whitney test	P-value
	Normal (n=10)	PV (n=14)		
LTB4 (pg/ml), median (IQR)	189.5 (148.4, 222.1)	428.4 (301.9, 484.6)	130	<0.001

The data are presented as medians and IQRs. Differences between groups were analyzed using a two-tailed Mann-Whitney test. IQR, interquartile range; LTB4, leukotriene B4; PV, polycythemia vera.

Table SIV. $CD34^+$ cells were incubated with different concentrations of zileuton for 14 days, and the numbers of CFU-GM and BFU-E colonies of $CD34^+$ cells from patients with PV (n=12) and healthy volunteers (n=10) were enumerated, % of control treatment.

	Normal (n=10)		PV (n=12)	
Group	CFU-GM, %	BFU-E, %	CFU-GM, %	BFU-E, %
A. 0 μM zileuton (control)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)
B. 50 μM zileuton	102.50 (90.95, 108.60)	98.32 (87.06, 103.70)	93.15 (82.48, 98.31)	85.02 (79.62, 92.15)
C. 250 μM zileuton	92.67 (88.12, 100.30)	90.66 (85.24, 95.68)	71.89 (59.23, 86.20)	53.59 (46.17, 72.45)
D. 500 μM zileuton	94.07 (85.78, 99.48)	86.22 (80.27, 98.04)	46.12 (33.62, 61.61)	19.59 (11.62, 36.65)
Friedman test				
Friedman statistic	5.400	4.920	32.700	33.800
P-value	ns	ns	<0.001	<0.001
Nemenyi post hoc test (P-value)				
B vs. A			ns	ns
C vs. A			<0.001	<0.001
D vs. A			<0.001	<0.001

Comparison of the effects of different concentrations of zileuton on the CFU-GM- and BFU-E-derived colony formation of normal bone marrow (n=10) and PV $CD34^+$ cells (n=12). Values are presented as medians and interquartile ranges. Differences among groups were analyzed using the Friedman test and the Nemenyi post hoc test was subsequently used for pairwise comparisons between groups. BFU-E, burst-forming unit-erythroid; CFU-GM, colony-forming unit for granulocytes and monocytes; ns, not significant; PV, polycythemia vera.

Table SV. Effects of treatment with 50 nM ruxolitinib combined with 100 μM zileuton on the CFU-GM- and BFU-E-derived colony formation of $CD34^+$ cells from patients with PV (n=12) and normal controls (n=10), % of control treatment.

	Normal (n=10)		PV (n=12)	
Group	CFU-GM, %	BFU-E, %	CFU-GM, %	BFU-E, %
A. Control	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)
B. 100 μM zileuton	99.79 (89.07, 108.40)	99.78 (92.42, 105.50)	88.25 (72.99, 92.88)	79.98 (69.15, 83.84)
C. 50 nM ruxolitinib	94.88 (86.22, 107.8)	89.23 (80.09, 99.26)	80.72 (66.75, 87.54)	65.08 (61.76, 76.94)
D. 100 μM zileuton + 50 nM ruxolitinib	80.95 (60.95, 102.00)	84.46 (75.03, 101.80)	63.68 (42.08, 71.99)	45.4 (36.63, 51.78)
Friedman test				
Friedman statistic	5.400	5.160	22.900	31.900
P-value	ns	ns	<0.001	<0.001
Nemenyi post hoc test (P-value)				
A vs. D			<0.001	<0.001
B vs. D			0.007	<0.001
C vs. D			0.040	0.018

The results are presented as medians and interquartile ranges. Differences between groups were analyzed using the Friedman test and the Nemenyi post hoc test was subsequently used for pairwise comparisons between groups. BFU-E, burst-forming unit-erythroid; CFU-GM, colony-forming unit for granulocytes and monocytes; PV, polycythemia vera; ns, not significant.

Table SVI. Effects of three treatments on the number of apoptotic cells in $CD34^+$ cells from patients with PV (n=10) and normal controls (n=6) after 2 days of treatment with 100 μM zileuton or 50 nM ruxolitinib alone or in combination, % of apoptosis.

Group	Normal (n=6), %	PV (n=10), %
A. Control	6.62 (5.07, 10.28)	6.01 (4.92, 8.47)
B. 100 μM zileuton	6.11 (5.07, 10.45)	8.52 (6.48, 10.48)
C. 50 nM ruxolitinib	7.14 (6.07, 10.83)	11.41 (8.28, 12.85)
D. 100 μM zileuton + 50 nM ruxolitinib	9.30 (6.83, 11.25)	19.15 (15.81, 21.44)
Friedman test		
Friedman statistic	6.600	34.900
P-value	ns	<0.001
Nemenyi post hoc test (P-value)		
A vs. D		<0.001
B vs. D		<0.001
C vs. D		0.040

Values are presented as medians and interquartile ranges. Differences between groups were analyzed using the Friedman test and Nemenyi post hoc test was subsequently used for pairwise comparisons between groups. PV, polycythemia vera; ns, not significant.

Table SVII. Effects of treatment with 100 μM zileuton and/or 50 nM ruxolitinib on cell cycle progression in $CD34^+$ cells from patients with PV (n=10) and normal controls (n=6), % of total cells.

	Normal (n=6)				PV (n=10)			
Group	Sub-G_0/G_1, %	G_0/G_1, %	S, %	G_2/M, %	Sub-G_0/G_1, %	G_0/G_1, %	S, %	G_2/M, %
A. Control	4.95 (3.33, 6.33)	60.70 (58.08, 63.58)	31.90 (29.70, 36.63)	0.95 (0.68, 1.25)	5.20 (3.90, 7.25)	59.20 (57.28, 62.50)	32.25 (30.50, 35.08)	1.30 (1.05, 1.73)
B. 100 μM zileuton	4.55 (3.20, 5.65)	60.75 (58.70, 64.70)	33.05 (27.90, 36.15)	1.00 (0.68, 1.65)	5.45 (3.60, 7.53)	64.70 (62.65, 66.35)	28.95 (24.53, 30.18)	1.10 (0.73, 1.88)
C. 50 nM ruxolitinib	5.25 (3.35, 6.03)	63.00 (58.95, 66.78)	29.30 (27.55, 35.18)	0.85 (0.40, 1.63)	5.65 (4.73, 8.28)	68.90 (67.65, 71.63)	22.30 (21.53, 24.33)	1.30 (1.13, 1.63)
D. 100 μM zileuton + 50 nM ruxolitinib	5.55 (4.55, 8.03)	64.95 (60.13, 66.98)	27.20 (24.68, 34.33)	0.90 (0.48, 1.05)	7.40 (3.83, 9.28)	79.15 (74.65, 81.00)	13.75 (10.68, 14.85)	1.20 (0.65, 1.90)
Friedman test								
Friedman statistic	6.939	6.000	7.080	1.021	4.900	24.300	26.700	2.847
P-value	ns	ns	ns	ns	ns	<0.001	<0.001	ns
Nemenyi post hoc test (P-value)								
A vs. D						<0.001	<0.001	
B vs. D						<0.001	0.001	
C vs. D						0.040	0.018	

The results are reported as medians and interquartile ranges. Differences between groups were analyzed using the Friedman test and the Nemenyi post hoc test was subsequently used for pairwise comparisons between groups. PV, polycythemia vera; ns, not significant.